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AUTOPLASTIC  
OVARIAN TRANSPLANTATION

And Its Clinical Significance.



By

J. H. NATTRASS, M.D., B.S.

Hon. Obstetrical Surgeon to the Women's Hospital, Melbourne.  
Late Hon. Clinical Assistant, Children's Hospital.

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From the Physiological Laboratory,  
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## Autoplastic Ovarian Transplantation and Its Clinical Significance.

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The possibility of removing the ovaries from their normal position in the female body and grafting them on to various other parts of the same or different animals, is a subject which has been receiving a lot of attention during the last few years from researchers in Europe and America.

Being exceedingly interested in the subject and desirous of seeing what would be the result of such experiments in our own laboratory,\* I determined to carry out a series of experiments in order to confirm or otherwise, and if possible to elaborate, the results previously obtained.

In the first place, I had to determine the most suitable animal on which to conduct these experiments. I found on examining the literature on this subject that rabbits had been most extensively used,<sup>1</sup> chiefly by Knauer, Limon, Grigorieff, Rubenstein and Foà, whilst Halban, Herlitzka, Schultz, and Ribbert experimented with guinea-pigs, Knauer, Marshall and Jolly with bitches; Halban used monkeys, Marshall and Jolly<sup>2</sup> used rats, and Guthrie<sup>3</sup> transplanted the ovaries of chickens. I found records also of five surgeons, viz., Morris,<sup>4</sup> Glass, Dudley, Cramer,<sup>5</sup> and Tuffier,<sup>6</sup> who had endeavoured to transplant ovaries in the human being. I decided in my experiments to work first of all with the bitch, chiefly because of the ease with which it could be obtained and kept, and because of its great resistance to anæsthetic and operative measures; but I soon found that because of the peculiar anatomical arrangement of its tubes and ovaries, it was quite unsuited for my purpose, the ovary being surrounded by a sac, formed by the dilated abdominal end of the tube, which made it difficult to know when it was completely excised<sup>7</sup>.

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\* I express my indebtedness to Professor Osborne for placing his laboratory at my disposal, and for much valuable advice; also to the Rev. W. Fielder, in whose department the microscopic sections were prepared, and Mr. W. J. Owens for the micro-photography.

I then tried the guinea-pig, and here the same objections prevailed, although not quite to the same extent.

I then resorted to rabbits. I found that they had an exceedingly poor resistance to shock following operations and were very poor subjects for chloroform. Of the first ones that I operated on, I lost two out of every three from these causes, but the anatomy of their tubes and ovaries was everything that I could desire; they were easy of access, clearly seen, and were easy to manipulate, although they were exceedingly small; however, these facts influenced me to persist in my efforts to overcome the disadvantages. Instead of giving chloroform as an anæsthetic, I tried rectal injections of Chloral Hydrate; this narcotised the animal completely, but in the absence of definite data to guide me in its use, I had to abandon it.

I then found that they would take ether well, especially if it were given on an open mask. In order to counteract the effect of shock following the operation, continuous heat seemed to be very necessary; if they were kept warm for some days by artificial means and well fed, the mortality was diminished to nil, in fact, my notes show not a single death recorded since this method of treatment has been adopted.

Having then determined to conduct these grafting experiments on the rabbit chiefly, I determined to acquire a thorough knowledge of the anatomy and of the macroscopic and microscopic structure of its ovaries. I therefore examined a large number in their normal state, in order that I could compare and contrast them with the grafted ovaries and be able to observe any alteration in size, weight or colour, or estimate any degeneration in structure.

## THE ANATOMY AND HISTOLOGY OF THE NORMAL OVARY OF THE WILD GREY RABBIT.

The ovaries of a rabbit, two in number, are situated one in each lumbar region, behind the kidneys, and one inch in front of the iliac crests<sup>s</sup>. They are generally about  $\frac{3}{4}$  of an inch in length,  $\frac{1}{4}$  of an inch in width, and  $\frac{1}{8}$  of an inch in thickness, oval in shape, pale yellow in colour, rough and miliary in appearance; greyish white projections can be seen on the surface at times, which are large ripe Graafian vesicles. They are attached to the posterior abdominal wall by the mesovarium, formed by a re-duplication of peritoneum, which is sufficiently long to permit of a considerable amount of ovarian movement. In every case the convoluted Fallopian tube extends forwards and outwards from each uterine cornu, passes behind the posterior extremity of its corresponding ovary, along its outer side

and then curves around the anterior end, becoming attached to it by its funnel shaped ostium; each ovary is well supplied with blood by the ovarian branch of the abdominal aorta, which can always be seen pulsating, where it crosses the lumbar muscles, transversely towards it.

The low power of the microscope shows the ovary to be fairly regular in structure, the greater part of it being composed of fibrous stroma rich in spindle shaped cells, blood vessels and nerves. The cortical part has a large number of Graafian follicles present in it, their arrangement in parts looking not unlike a string of beads in the peripheral tissue; the follicles vary much in size, the larger ones being deeper in the stroma than the average ones. Very large ones are sometimes seen ready to burst superficially. In pregnant animals corpora lutea can always be demonstrated.

With the high power the germinal epithelium and egg tubes can be made out, and the various parts of the Graafian follicles, *i.e.*, the germinal vesicle with the germinal spot, the vitellus, the zona pellucida, the discus proligerus, the membrana granulosa and the surrounding theca folliculi are all easily seen.

## THE AUTOPLASTIC TRANSPLANTATION OF OVARIES.

*Experiment 1.\**—The abdomen of a three-quarter grown doe was clipped free from hair, washed and cleansed with perchloride, ether was given on an open mask and abdominal section performed.

The left ovarian artery was tied and the left ovary excised and placed in normal saline; a small incision was then made, through the peritoneal and capsular covering of the left kidney; a small part of the capsule was freed from the renal tissue; the ovary was then passed through the incision under the capsule and was thus retained in close proximity to the renal tissue; the incision was then sewn up with fine silk.

The right ovary was excised in a similar manner, and the skin being well retracted from the edge of the abdominal incision, it was sewn on to the outer surface of the right external oblique muscle. The abdominal wound was then closed with silk-worm gut and the rabbit placed in an artificially heated hutch.

A.—Fourteen days later under ether the subcutaneous graft was removed:—The ovary was well defined and felt quite firm, more white in colour and seemed to be slightly larger

\*These experiments were carried out between December 9th, 1908, and August 16th, 1909.

than normal; it was hardened in 10 per cent. solution of Formalin in spirit, stained with alum carmine, embedded in paraffin and cut in serial sections; when viewed with the eye, the sections seemed to belong to some hollow viscus, because the central part for some reason had failed to take the stain.

Examined under the microscope, the following features were observed:—

1. The most striking change is found in the cells of the fibrous stroma, which are much enlarged and granular; this condition is most marked in the centre of the specimen, which has also failed entirely to take the alum carmine stain and presents a greyish yellow appearance; surrounding this central part in most of the sections is an irregular circle of over-stained tissue, in which the cell shape can not be made out and nothing can be detected but deeply stained granules. (Figure 1.)

2. The tissues of the periphery seem normal; Graafian vesicles, large and small and egg tubes can be demonstrated in abundance, they seem little if at all altered, and their structure can be clearly made out.

3. Even at this early stage, commencing organization between the graft and adjacent tissue can be easily demonstrated. Many tufts of fine fibrils can be seen passing transversely from some of the peripheral cells of the ovary to the subcutaneous fascia.

B.—Twenty-eight days after the grafting operation, the rabbit's abdominal cavity was again opened under ether and the left kidney excised. The grafted ovary was seen beautifully in position, whitish yellow in colour; it showed up distinctly against the dark red renal tissue; it felt quite firm and seemed slightly larger than normal; three large greyish vesicles could be seen on its surface, which even with the naked eye could be recognised as Graafian follicles ripe and ready to burst.

Under the microscope:—

1. The central part of the ovary is unstained, is yellowish white in colour and contrasts with the tissues of the periphery, which are stained pink. The outline of the cells is usually indistinct, and in places nothing is seen but a mass of granules; towards the periphery the shape of the cells can be made out though much swollen and granular; in the tissue surrounding the unstained part is seen an excess of deeply stained cells, like leucocytes, which in places have migrated, probably along lymph spaces, into the centre of the specimen, and are seen as columns or irregular patches.

2. A similar specimen counter-stained with osmic acid gives a brown or a dark coloration to a large part of the centre of the ovary, showing the presence of fatty degeneration.

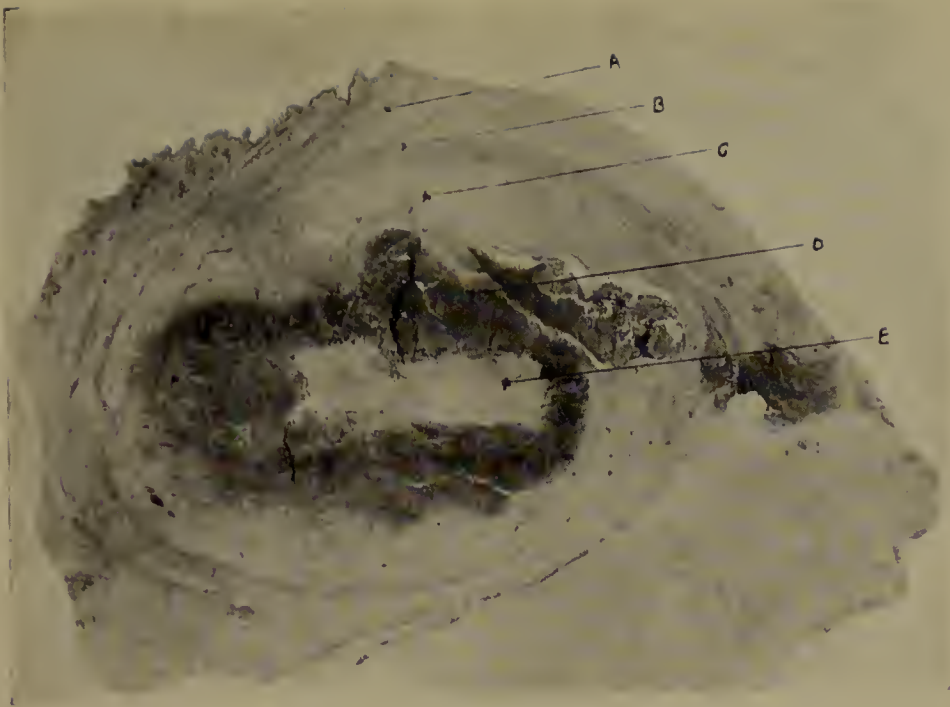


FIGURE 1. (Experiment 1A.)

Showing degeneration in a 14 day subcutaneous graft.

- A. Subcutaneous tissue.
- B. Circumference of ovary.
- C. Egg bearing part of ovary.
- D. Degenerated tissue over-stained.
- E. Degenerated tissue unstained.

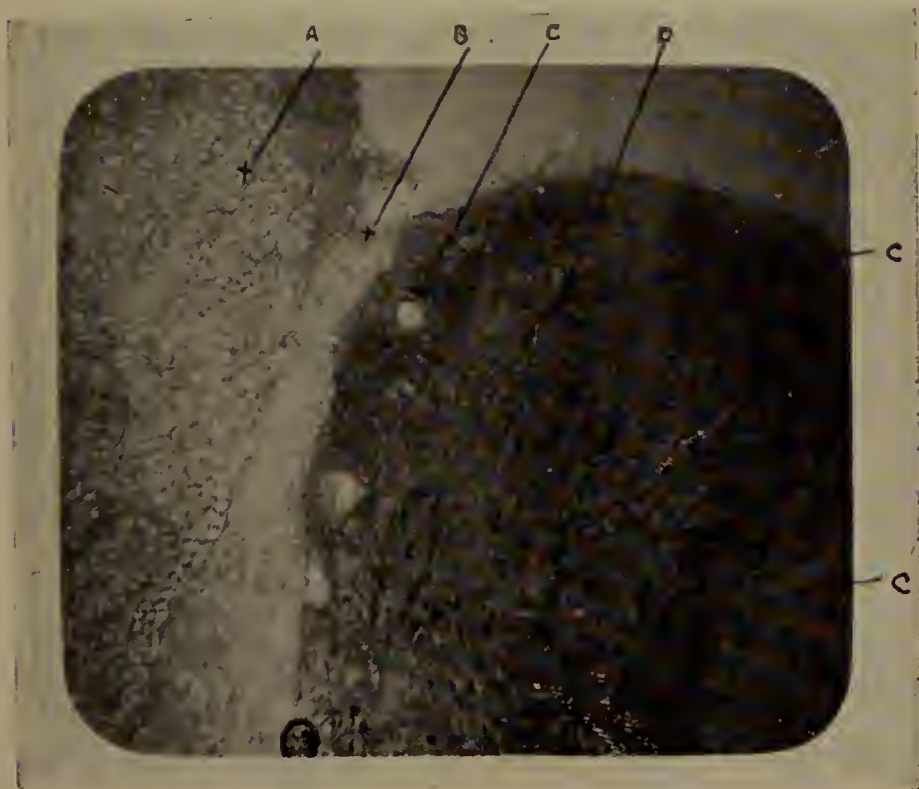


FIGURE 2. (Experiment 1B.)

Showing dense fibrous adhesion in a 28 day ovario-renal graft.

- A. Renal tissue.
- B. Dense fibrous adhesions.
- C. Graafian vesicles.
- D. Ovarian tissue.

3. Large and small Graafian vesicles and egg tubes are present in the peripheral tissue, and appear quite normal in structure.

4. The ovary has become adherent to the kidney by a narrow band of fibrous tissue, which can be seen to dip down in places, between the groups of renal cells. The permanent nature of the union is best seen in the angle formed by the margin of the ovary with the kidney where it is supplemented by the renal capsule. (Figure 2.)

The microscopical examination of these early grafts is full of interest, as they indicate the pathological changes that do occur in such a tissue transplantation, and provide us with data from which to reason, and so guide us in our future efforts. The fibrous stroma of each grafted ovary underwent fatty degeneration; it appeared to be more extensive and more intense in the subcutaneous graft than in the renal one, where it was obviously undergoing absorption and repair as indicated by the migration of white cells into it, this being probably due to the kidney being more vascular than the subcutaneous tissue.

In each specimen the peripheral tissue was the least affected; the egg tubes and Graafian vesicles persisted and continued to develop and mature. In the fourteen day graft commencing adhesion to adjacent tissue could be observed with the high power; in the twenty-eight day graft it was abundant and complete.

*Experiment 2.*—In this, Experiment II B was practically repeated, except that in this instance each ovary was transplanted on to its corresponding kidney, and that instead of being placed under the peritoneal and capsular covering of the kidney, they were fixed by fine silk, on top of those membranes. The rabbit was kept for 195 days and then destroyed and the grafts examined.

That on the left kidney had in part been absorbed; about half of it still remained; it was pale yellow in colour and felt firm.

That on the right side had become adherent to the under surface of the liver, but the pale yellow graft could be easily seen, showing between the renal and hepatic tissue.

Under the microscope:—

Graafian vesicles large and small are present in the left graft, large ones being present only in the right; there are dense fibrous adhesions to the kidney in each, and on the right side to the liver also; in the centre of the right ovary there is a hyaline patch of tissue with granular cells scattered through it, the remains of fatty degeneration; there is no trace of this in the left ovary.

This experiment is interesting because the graft has lived in its new location for 195 days. Its adhesions to the kidney are dense and firm, particularly on the right side, where it is adherent to the liver also. The area of degeneration is absent in the sections examined in one, and very small in the other.

*Experiment 3.*—In this, Experiment 2 was repeated, the ovary being again sewn on to the peritoneal and capsular covering of the kidney. In the previous experiment, the fibrous union of the graft to the adjacent tissues was most evident. In this instance I desired to show that vascular union is also established, the following being the method of procedure.

After the transplantation, the rabbit was kept for 167 days. It was then killed and rapidly skinned. Abdomen and thorax were opened in mid-ventral line. The heart was observed to be still beating. The descending thoracic aorta was then picked

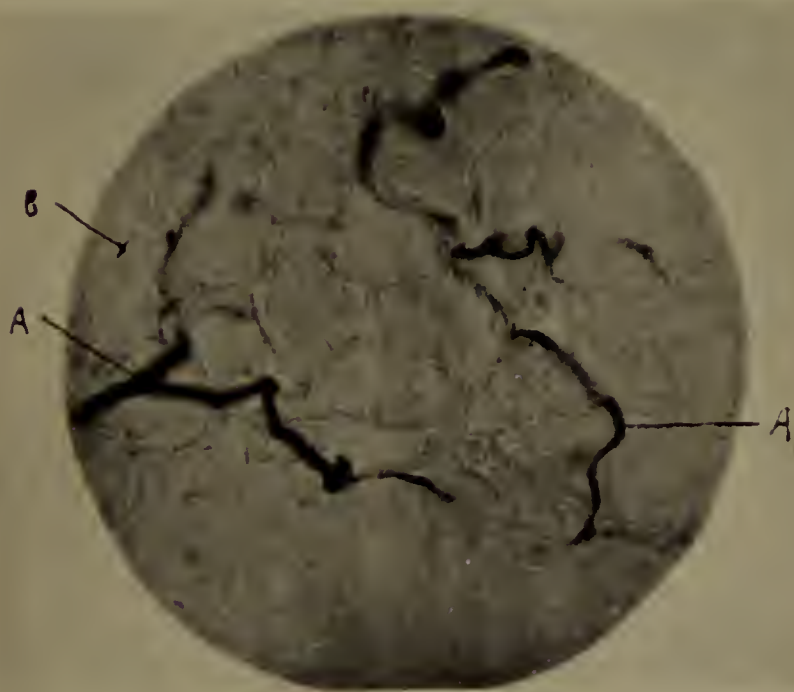


FIGURE 3. (Experiment 3.)

Showing blood vessels which have developed in an ovario-renal graft in 167 days.

up with a threaded aneurism needle. An incision was then made in the aorta, nearer the heart than the ligature; a cannula was inserted and the ligature tied around the cannula. Normal saline at 98.4 deg. F. was now forced through the arterial system. The Inferior Vena Cava was incised to allow the escape of blood; the parts whose blood supply was below the inserted

cannula soon became blanched. After ligation of the abdominal aorta, just before its bifurcation into the iliacs, a solution of carmine was injected in a similar manner; the kidneys thus became engorged with carmine jelly and appeared pink in colour. The renal artery was now tied, the kidney excised and prepared for serial section.

*Microscopic Examination:—*

Showed the presence of a considerable number of fairly large blood vessels in the graft. As they were either stained with, or contained the carmine jelly, they stood out plainly and were easily seen. (Figure 3.)

This experiment was not so successful as it could have been, owing probably to some slight error in technique, or perhaps in the preparation of the carmine jelly, but the result showed the presence of a considerable number of blood vessels, which would be more than sufficient to provide the graft with an abundant blood supply.

*Experiment 4.*—A three-quarter grown doe was prepared in the usual way, was etherized and abdominal section was done; the left ovary was removed and transplanted on to the free extremity of the spleen; the spleen bled freely, but it was easily controlled with gentle pressure.

The right ovary was excised and grafted subcutaneously on to the outer surface of the right external oblique muscle of the abdomen.

197 days later the rabbit was killed and the grafts examined.

The splenic graft was quite hidden by fatty adhesions which surrounded it entirely, but when these were removed, the ovarian tissue, yellowish white in colour, stood out quite plainly against the dark red spleen; it appeared normal in size, shape and colour.

The microscopic section shows the following:—

(1) A large number of Graafian vesicles of varying sizes are seen, as many as three large ripe ones can be found in one section, and others varying in size from the smallest recognizable. Egg tubes are present; corpora lutea can be seen in some. A noticeable feature is that most of the follicles are present in the periphery adjacent to the spleen. (Figure 4.)

(2) In the stroma of some sections is found a hyaline patch, with clumps of granules scattered through it, but in most there is no evidence of fatty degeneration, except that there seems to be a little more fibrous tissue than normal.

(3) The ovary is firmly adherent to the spleen by a thick broad band of fibrous tissue.



FIGURE 4. (Experiment 4.)

Ovario-splenic graft 197 days.

The dark part on the left of the picture is the spleen, the tissue on the right is the ovary showing large Graafian vesicles.

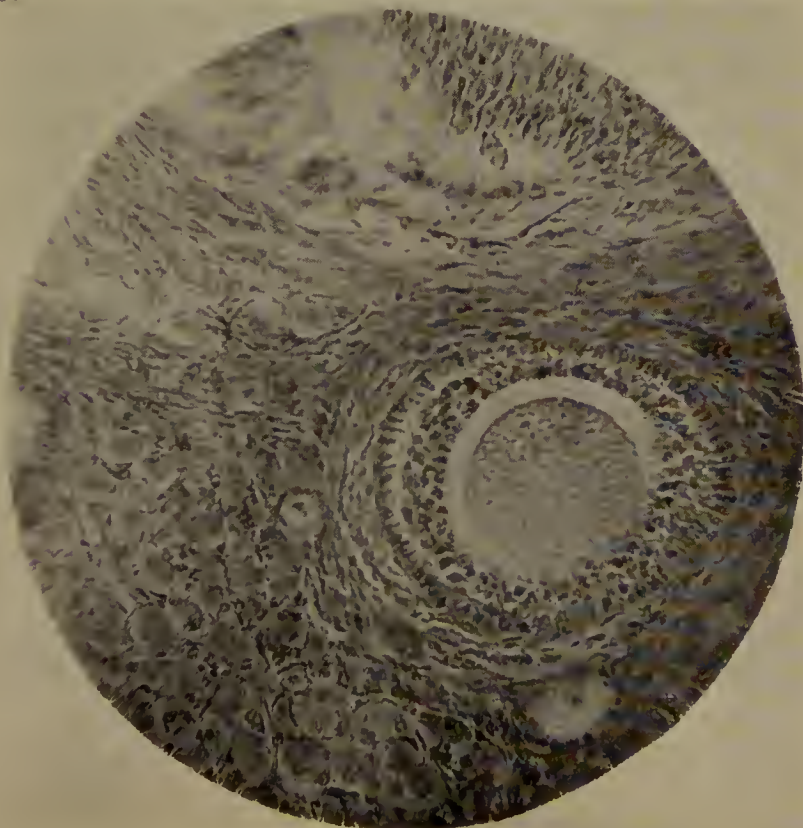


FIGURE 5.

A high power photo. of a small Graafian vesicle in Figure 4.

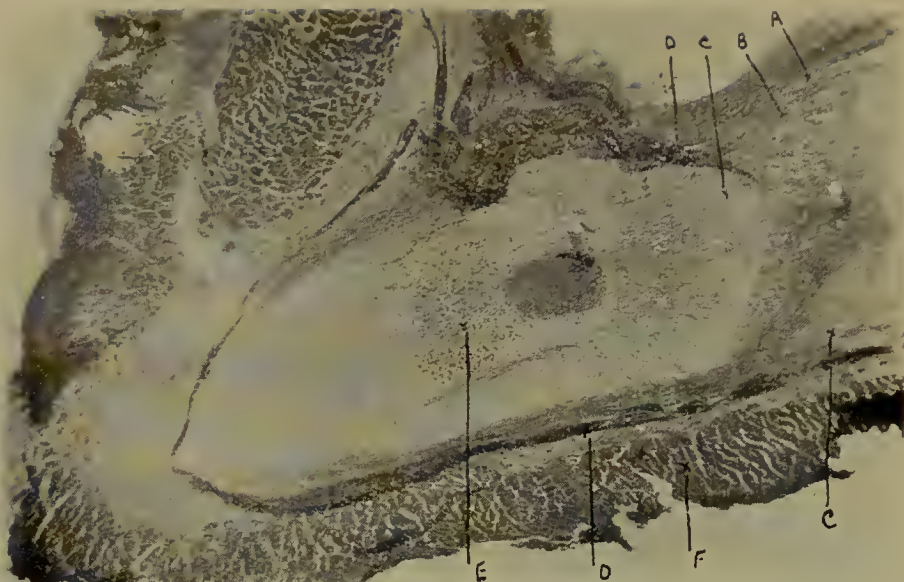


FIGURE 6. (Experiment 4.)

A subcutaneous graft of 197 days.

- A. Subcutaneous tissue.
- B. Graafian vesicles.
- C. Ovarian tissue.
- D. Ribbons of striated muscle.
- E. Area of degeneration.
- F. Abdominal external oblique muscle.



FIGURE 7.

A high power photo. of the Graafian vesicles B in Figure 6.

The ovary grafted on the outer surface of the external oblique muscle had become divided into three parts (probably by my ligatures); they were granular on the surface, yellowish white in colour, and felt firm. (Figure 6.)

Under the microscope:—

(1) Graafian vesicles large and small may be seen.

(2) Fibrous adhesion to adjacent tissue is strongly developed. A peculiar feature is, that ribbon-shaped strands of skeletal muscle fibre seem to surround the circumference of the ovary; the spindle shape of the muscle fibre is beautifully seen, the rest of the muscle being cut transversely. (Figure 6.)

(3) The central part of the ovary has not yet completely recovered from the condition of fatty degeneration; it presents now a hyaline appearance, with large round-looking cells scattered through it, the cells being exceedingly granular. The hyaline part stains very feebly; it is not nearly so extensive in area, as the area of fatty degeneration in the previous subcutaneous graft. (Experiment 1A.)

The points of interest in this experiment are:—That the ovaries have survived for 197 days after transplantation, and that in their new location they have still continued to develop and mature their Graafian vesicles. The remains of fatty degeneration are less in the splenic than in the subcutaneous graft, probably because the spleen is much more vascular than the latter tissue. The degenerated area in the subcutaneous graft is much smaller than in a similar graft of less duration, showing that absorption and repair have been proceeding rapidly.

*Experiment 5.*—Abdominal section was performed on a half-grown doe. The left ovary was excised and placed in normal saline at 98.4 deg. F. The right ovary was then removed and placed in the exact position of the left, being fixed to the peritoneum and underlying muscle. The left ovary was then placed in the position of the right in a similar manner; in doing this great care was taken not to injure the tubes nor disturb their anatomical arrangement.

The ovarian arteries were tied about one inch from the ovaries.

After 97 days the rabbit was killed and the ovaries examined. Bowel is adherent to the situation of each. The ovaries have been absorbed to such an extent that it is difficult to say if any exists at all on the right side, but the left can be felt, although very small.

Microscopic Section shows:—

The presence of ovarian tissue on each side, and each is crowded with Graafian vesicles, large and small. A noticeable

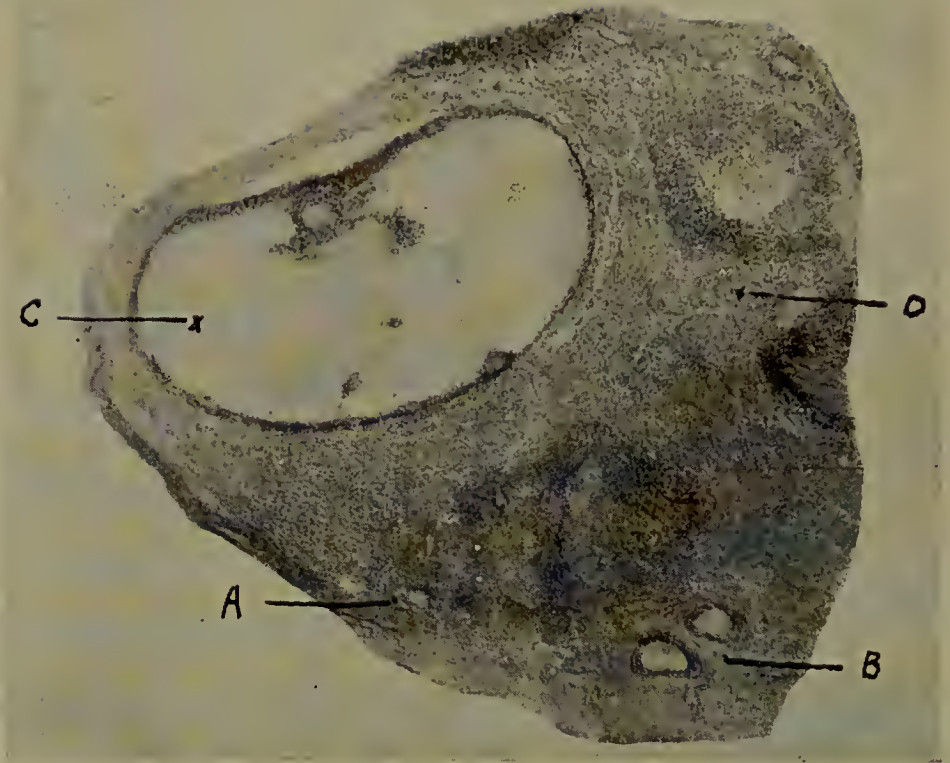


FIGURE 8. (Experiment 5.)

Right ovary transplanted on to the position of the left. (For 97 days).

- A. Very small Graafian vesicle.
- B. Graafian vesicle.
- C. Large ripe Graafian vesicle.
- D. Ovarian stroma.

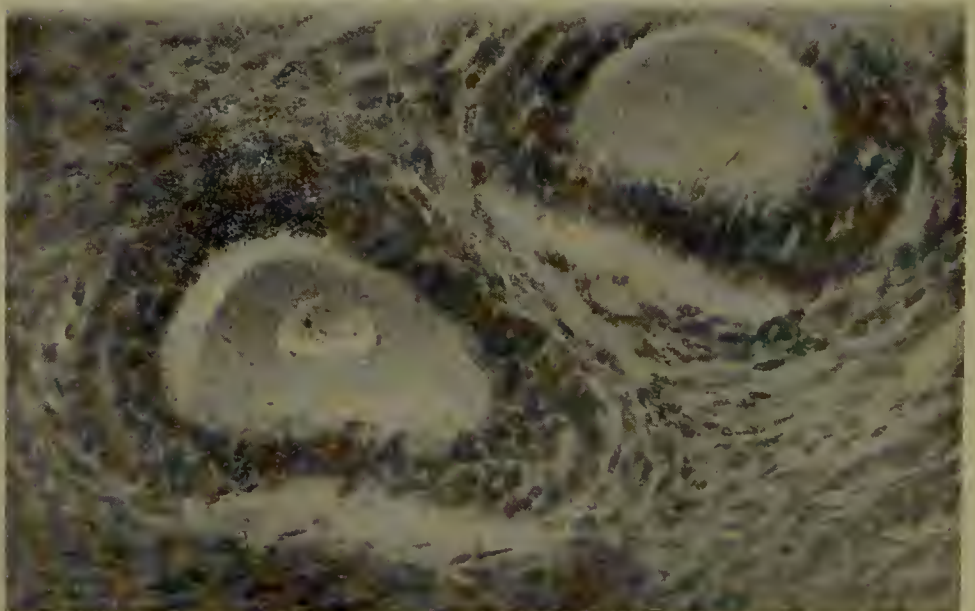


FIGURE 9.

High power photo. of Graafian vesicle B in Figure 8.

feature is the small amount of stroma in comparison with that of other grafts, also it is small in proportion to the number of vesicles. (Figures 8 and 9.)

The absorption of these ovaries is remarkable, and I think is due most probably to tying the ovarian artery so far away from the seat of the graft, as the blood supply would then be cut off from the large area of tissue which the artery supplies; this would have an injurious effect on the graft, by minimising its supply of nourishment, resulting in greater degeneration and consequent absorption.

*Experiment 6.*—In this experiment, the ovary was grafted on to the periosteum of the seventh rib. After 167 days the rabbit was killed. The ovary could be felt lying snugly in the intercostal space. The 6th and 7th ribs with intervening muscles were removed, the bony part of the ribs was shelled out of the periosteum, and microscopic sections prepared.

Examination showed several large ripe Graafian vesicles, also some small ones (Figures 10 and 11). Fatty degenera-



FIGURE 10. (Experiment 6.)

Ovary grown on the periosteum of the seventh rib and external intercostal muscle for 167 days.

- A. Space where the rib was.
- B. The periosteum peeled off the rib.
- C. External intercostal muscle.
- D. Intercostal artery, vein and nerve.
- E. Ovarian tissue.
- F. Large Graafian vesicle.
- G. Small Graafian vesicle.

tion has disappeared, and a slight increase of fibrous tissue was the only indication that it ever had been present. The adhesion of the ovary to the periosteum of the rib is seen most plainly; it is also attached to the adjacent intercostal muscle. (Figure 10.)

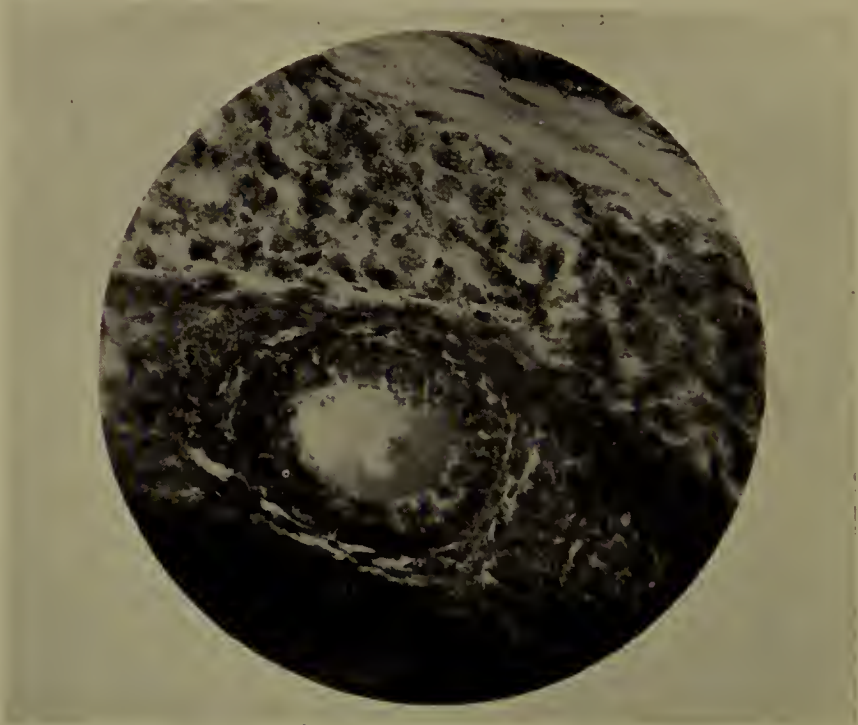


FIGURE 11.

A high power photo. of Graafian vesicle "G" in Figure 10.

My object in growing the ovary on the periosteum of the rib is not only to increase the number of tissues on which the ovarian grafts have been grown, but also to demonstrate the suitability of the intercostal spaces for these grafting purposes. The vascular periosteum and intercostal muscles provide abundant nourishment for the transplanted tissue, whilst the bony ribs afford it much protection from injury and undue pressure, and its superficial position renders it most easy of access.

*Experiment 7.*—The left ovary of a full grown doe was removed from its normal position and was transplanted on to the uterus on its ventral surface, at its point of bifurcation into right and left cornua. The right ovary was also excised and was grafted on to the outer surface of the right abdominal external oblique muscle.

The rabbit was subsequently placed in the hutch with a buck, 129 days after the grafting operation, it was discovered to be pregnant, and four days later it gave birth to a family of four young ones.

Seven weeks later, it was killed and the grafts examined; the right ovary which had been placed in the right external oblique muscle, could not be found; the left one, which had been put on the uterus, persisted only as a scar.

On examining the original ovarian sites, it was discovered, that when tying the left ovarian artery at the time of the operation, a small piece of the ovary had become involved in the knot of the ligature, and this had become hypertrophied until it was about one quarter the size of a pea, and this had undoubtedly given rise to the ovum which had produced the foetation.

*Experiment 8.*—In this experiment the right and left ovaries were excised and were transplanted on to the peritoneum lining the anterior abdominal wall. 173 days after the grafting the animal gave birth to two young ones, then 26 days later to another family of four, premature ones. The rabbit was subsequently killed and examined. Both the grafts had become absorbed, all trace of them had completely disappeared, except for some remains of the silk ligatures; as in Experiment 7 a small piece of ovary was found involved in the knot tying the ovarian artery on each side.

These two experiments are exceedingly interesting, as they are the only ones in this autoplasmic group, where complete absorption of the graft has occurred.

As they are the only ones in which the oophorectomy was incomplete, the question immediately suggests itself, as to whether the remnant was the cause of the absorption of the grafts or not.

Crowe, Cushing and Homans,<sup>9</sup> working at transplantations of the pituitary body, found that, in order to get the best transplantation results, that gland had first to be completely excised from its normal position; if this were not done, their transplantations were more or less unsuccessful. These observations made by them regarding the pituitary transplantations, concur exactly with these results, obtained by me in ovarian transplantations. In all my experiments, without exception, where the ovaries were completely removed from their normal position, and transplanted elsewhere in the body, the grafting was accomplished so successfully that functional ovaries resulted, but in each case, *i.e.*, Experiments 7 and 8, where the excision was incomplete, absorption of the grafts occurred.

It would appear from a consideration of these results that complete excision of a gland, yielding an internal secretion, creates in the body a physiological want, and then even a grafted gland is welcomed by the organism as a factor having power to supply the want; but if the excision were incomplete, the remnant has the power to supply the needs of the body, and then any graft being superfluous, the protective agencies regard it as a foreign substance and remove it.

Another feature of interest in these two experiments (Experiments 7 and 8) is the great hypertrophy of the little piece of ovary, which had been left behind. At the time of the operation, it was so small as to completely escape notice, but when subsequently examined it was quite appreciable in size. This fact is in accord with the results obtained by Carmichael and Marshall,<sup>10</sup> who found that, if portions of ovaries were removed, compensatory hypertrophy always occurred. In one instance cited by them, one-fifth only of an ovary was left behind. Six months later, it weighed 0.37 grams; that is, it was larger than the average weight of a whole ovary in an adult rabbit. This hypertrophy displays an inherent ability on the part of the ovary to adapt itself to the individual requirements of the body, and to provide a supply of hormone secretion equal to the demands made upon it, the extent of hypertrophy apparently being the amount of secreting tissue necessary to permanently adjust the physiological balance.

It may be claimed that this equilibrating power, displayed by the living organism has a far reaching significance, both physiologically and pathologically.

*Experiment 9.*—The ovaries of a fox terrier slut were removed from the abdominal cavity—the right one was transplanted subcutaneously on to the right abdominal external oblique muscle—and the left one was placed in the sheath of the left abdominal rectus muscle.

370 days later abdominal section was done and the original ovarian sites examined. This was very difficult, owing to the presence of a lot of adhesions—but no ovarian tissue was found. The grafted ovaries were then removed and examined.

That on the external oblique muscle was several times larger than normal; it felt semi-fluctuant, and did not look like ovarian tissue.

Microscopically:—

Its cells were all swollen very much, and looked as if they had undergone colloid degeneration; it could not be recognised as ovarian tissue. One distinctive feature was the large number of blood vessels, full of blood, which coursed through it.

That in the sheath of the rectus muscle was smaller than normal, was flattened out, and yellowish white in colour, and was firmly adherent to the muscle surrounding it.

Sections showed:

(1) Some large Graafian vesicles; a great number of smaller ones of varying sizes, but altered in shape, their sides being pressed together in such a way that the cells of the membrana granulosa are arranged as columns or cylinders. Egg tubes are also present. (Figures 12 and 13.)

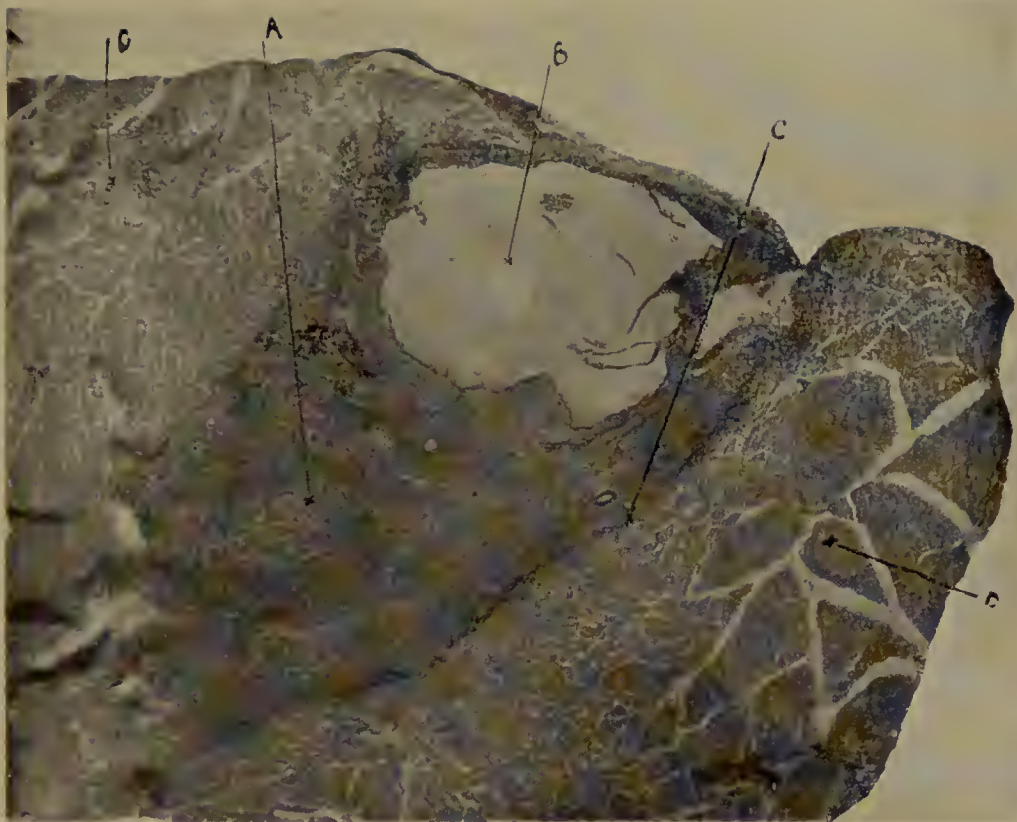


FIGURE 12. (Experiment 9.)

An ovary transplanted into the left abdominal rectus muscle of a bitch for 370 days.

- A. Ovarian stroma.
- B. A large Graafian vesicle.
- C. A great number of small Graafian vesicles and egg cells.
- D. Rectus muscle.



FIGURE 13.

A high power photo. of small Graafian vesicles ("C" in Figure 12).

(2) Fibrous adhesions are firm and definite.

(3) No definite evidence of the existence of fatty degeneration can be made out.

The bitch was used in this experiment, in order that observations could be made regarding the presence of sexual heat. After the ovaries had been grafted, it was found that the slut came on heat three times during the year, each period being characterised by the usual phenomena, *i.e.*, vulvovaginal swelling, sanguineous moisture and distinct inclination towards the dog, clearly showing that the ovaries although growing in this abnormal position, still continued to perform their oestrous functions.

## CONCLUSIONS FROM THE ABOVE EXPERIMENTS.

(1) That it is possible to remove the Ovary from its normal position in the female body and to transplant it on to other tissues. In the experiments described above they were successfully grafted on to the kidney, spleen, subcutaneously on the external oblique muscle, on the peritoneum, periosteum and the external intercostal muscles.

(2) When the transplanted ovary is examined in the early stage, it is found to be firm in consistence, whiter and slightly larger than normal. This is shown by the microscope to be due to swelling of the cells of the stroma, which have undergone fatty degeneration.

This degenerative change is found to be present in most of the specimens examined. The amount seems to be inversely proportional to the vascularity of the tissues receiving the graft, and directly proportional to the thickness and density of the graft itself. Thus there was more degeneration in a subcutaneous, than in a renal or splenic graft. This is in accordance with the observations of Knauer, who states that in his experiments a portion of the ovary always died—but differs from the experience of Marshall and Jolly,<sup>11</sup> who maintain their belief "that it is possible to graft an entire ovary autoplastically without any part of it dying."

In the older grafts there is a diminution in the size of the ovary. There is an increase in the amount of fibrous tissue, a progressive absorption and repair of pathological products, a continued development of egg cells, and production and maturation of Graafian follicles, although not nearly to the same extent as in the normal ovary.

(3) The grafts become firmly adherent to the adjacent tissues by dense fibrous bands; the development of these adhesions can be studied easily in a fourteen day graft (Experiment IA), when even with the low power, thick bunches of

fibrils can be seen passing transversely from the ovary to the adjacent structures. In a twenty-eight day specimen (Experiment 113), the fibrous union appears complete.

(4) The graft when placed in its new position is undoubtedly nourished by transudation of fluid from the lymph spaces of the adjacent tissue, hence the periphery of the ovary, or the egg-bearing part, always retains its vitality; but later, blood vessels become developed and vascular union established (Experiment 3), the graft thus receiving blood from the arterial system.

(5) The slut in Experiment 9, whose ovaries were removed from the abdominal cavity and were grafted, one on the external oblique muscle, and the other in the sheath of the rectus muscle, repeatedly showed all the symptoms of sexual heat, *i.e.*, vulvovaginal congestion, sanguineous discharge, and was warded by the dog, showing that the ovaries, even though in this abnormal position, continued to carry on their functions as organs of internal secretion and to regulate the sexual life of the animal.

## THE CLINICAL SIGNIFICANCE OF \*AUTOPLASTIC OVARIAN GRAFTS.

The autoplasmic grafting of ovaries is a measure that ought to take its place and fulfil a definite purpose in the world of conservative Gynecological Surgery. Although obviously hedged in by limitation, it has no such wide field of usefulness as a homoplasmic graft would have, yet in some specialised cases, the value of it is apparent. The simplicity of technique, the ease and rapidity with which a graft can be done, does not prolong an operation more than a few minutes, and would not materially increase the attendant shock. The immense benefit that may be derived by the patient more than justifies the surgeon in attempting it, and then, should complete success crown his efforts, the result is only another triumph of the science of surgery in the interest of suffering humanity.

With our present knowledge of the function of the ovary and the profound influence its secretion has on the whole female organism, it should be an axiom always among all Gynecologists, "that the functional ovary should never be excised from the body, without definite indications, and when

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\*The term "Autoplasmic Graft" is used to indicate that an animal's own ovaries are grafted on to itself. "Homoplasmic Graft" is used when grafting from one animal on to another of the same species, "Heteroplasmic Graft" being reserved for grafting from one to another of a different species. This nomenclature differs from that used by some writers.

those indications for its removal are present, the question of doing an autoplasmic graft should always be considered."

The following are instances where such considerations may be necessary:—

## (1) OPERATIONS FOR UTERINE DISEASE.

(a) In Hysterectomy for large fibroid tumours. In removing the uterus for even fairly large fibroids, it is usually easy to do so in such a manner as to leave one or both ovaries intact, but no matter how conservative the surgeon desires to be, he will meet with some cases where it is impossible, or at all events unwise to carry out these principles. A large interstitial myoma, or large myoma in the broad ligaments may stretch the ovary over its surface, or involve it in such a way that it cannot be left behind, and its removal would be the only course the operator may have.

(b) In Hysterectomy for uterine Carcinoma. In this operation, as in that for fibroids, in a large number of cases, it is comparatively easy to leave the ovaries intact, but when there is any suspicion of the tumour having extended beyond the uterine tissue, the surgeon is necessarily anxious to remove as much of the pelvic contents as possible, and very correctly should not stultify the results of his operation for the sake of trying to save the ovaries; but in some cases where there is a reasonable hope of their being free from infection, whilst it is not wise to leave them in the pelvis, it would be safe enough to graft them subcutaneously in any accessible part.

(c) In Vaginal Hysterectomy for uterine prolapse. In removing the uterus for cases of moderate prolapse, it is usually easier to leave the tubes and ovaries than to remove them, but in some of the most severe cases, the uterus in its descent has by continuity of tissue dragged the adnexa downwards with it. Their extreme displacement and mobility then raises the question of the wisdom of leaving them, as they may project into or through the wound, or may become adherent in some abnormal position, which might produce troublesome symptoms.

In such operations as the above, the only course open to the operator is to remove the ovaries in addition to the tubes and uterus. The standard text books of Gynæcology describe this procedure as the proper one in such cases. If the patient is in the period of sexual activity, then she not only undergoes the shock attendant on such a big operation, but in addition has to bear the full force of climacteric symptoms also, which would be induced by the removal of the ovaries. The contention of this contribution is, that in all such cases an attempt should be made to graft the ovaries somewhere in the body,

as experimental evidence points out, that after transplantation the ovaries still continue their functions.

## (2) IN OVARIAN DISEASE.

(a) In double cystic disease of the ovaries, it is the usual practice when the cysts have developed to any size, to perform double oophorectomy. This, when the ovaries are functionally active, is always a serious matter, as it not only completely removes the possibility of reproduction, but what in some cases is more important, it deprives the body of the ovarian secretion, which seems so essential to it, and which exerts such a powerful influence upon it. In the light of our present knowledge, we can say that such a drastic procedure is not always the best that can be done, as there are certain cases where with proper discrimination, the whole or at all events a part of the ovary may be saved, by separating it from the cystic part and transplanting it back again to its original situation or grafting it on to any other vascular part of the body.

For the purpose of description in such a case, let it be assumed that the whole of one ovary is involved to such an extent by a large cyst (Adenoma, Cystoma, or Dermoid,) as to necessitate its complete removal, and that the other one is affected with one of the following conditions:—

(1) In simple cysts of the oöphoron. In cases where the cyst is very small, an incision into it, evacuation of its contents and a few stitches to guard against hæmorrhage are all that is necessary, the ovary being left otherwise intact; but when the cysts are larger, it becomes necessary to remove the ovary entirely. In these it is sometimes possible to obtain a portion of the egg-bearing tissue, which would be sufficiently large to be worth transplanting into the body again.

(2) In cysts of the paroöphoron. The same remarks apply to these as to simple cysts, except that they, growing from the hilum tissue, may permit of obtaining a greater amount of the oöphoron for transplantation, their papillomatous condition always assisting in their diagnosis.

(3) Cysts of the parovarium. This is one of the best lesions for obtaining the ovary for grafting purposes, and forms about ten per cent. of all cases of cystic ovary<sup>7</sup>. Situated as they are between the layers of mesosalpinx, they rarely attain large size, are usually unilocular and have the stretched tube above them, and the ovary attached to their wall, it thus being easy to recognise and remove.

In each of these cases the portion of the ovary so obtained could be transplanted, either on to the situation from which it has just been removed, or if there were any doubt about it

developing more cysts, it could be placed subcutaneously in any convenient position in the body. If it were replaced in the normal position again, and if the operation had not injured or displaced the tube in any way, the graft continuing to develop Graafian vesicles, would make reproduction of the species still a possibility. (Experiment 5.)

These remarks apply directly to all females up to the period of the climacteric, but especially do they apply to females before puberty. To remove both ovaries from a child before menstruation is established means that it will retain a male-like form and fail to develop some of the secondary characteristics of her sex<sup>1</sup>. But if a portion of ovarian tissue could be successfully grafted, then it is reasonable to suppose that it would still continue to exert its influence on the general metabolism of the body, and the usual female form would be the result.

The slut in Experiment 9, whose ovaries were growing for 370 days outside the abdominal cavity, at intervals during that time displayed all the phenomena of sexual heat, *i.e.*, swollen vulva, sanguineous discharge, and attraction for the male, and was warded by the dog frequently. By analogy, the human ovaries, even though growing in abnormal positions, would still continue to control the sexual life of the individual.

(b) In the following cases of intractable dysmenorrhœa, the transplantation of the ovaries to some other part of the body may be of great benefit to the patient.

(1) In neuralgic dysmenorrhœa: this is usually found in females of exceedingly neurotic temperament, although no actual disease can be detected, yet at every menstrual period the patient habitually suffers pain, which in some cases is sufficiently severe to break down the general health, and to completely disorganise the nervous system. Treatment by drugs is of little or no avail, and the patient's life is rendered unbearable by the intensity of her suffering.

(2) In ovarian dysmenorrhœa, pain is not only experienced during menstruation, but frequently occurs in the intervening interval. Associated with it can be felt enlarged, tender and prolapsed ovaries. As in the neuralgic form, the frequency and duration of the suffering debilitates the patient to such an extent, that the gravest results are possible. Hysteria Gravior, Epilepsy, and even Mania<sup>12</sup> are known to supervene sometimes.

In such cases as the above, therapeutic agents are taxed to their very utmost, and often the most powerful analgesics, fail to give more than a transient relief, and sometimes not even that.

Then, as a last resort, text-books recommend that double oöphorectomy should be performed, but experience shows that the results obtained from this procedure have not been altogether too satisfactory, a probable cause being that the constitution, already deviated by ill-health, and the nervous system disorganised by suffering, although it is able to bear the shock of the operation, is not able to bear the sudden force of an artificially produced climacteric, and when, after this operation, its phenomena develop with suddenness and severity, the condition produced is almost as bad as that for which relief is sought.

Because of knowledge gained experimentally, it is here urged, that in these intractable cases, the ovaries should not be sacrificed in this manner. Let them be removed by all means from the situation where the neuralgic ones have been in the habit of producing pain, and where those producing ovarian dysmenorrhea have converted a physiological vaso-motor dilatation, into a pathological congestion, swelling and tenderness, but let them be again transplanted on to some other tissue of the body, and although this at once destroys their power as organs of reproduction, they would still be able to yield to the body that secretion, which is so essential to the well-being of every female in the reproductive period of life, and thus the onset of the climacteric would be delayed indefinitely, with proportional benefit to the patient.

(c) In those cases where it is desired to induce sterility, as contraction of pelvis, deformed pelvis, etc., transplantation of the ovaries is submitted as an alternative to the present method of treatment.

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